

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Claim 1. (Original) A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian heparanase protein, the sequence of nucleotides comprising two consensus cleavage sites recognized by an endoproteinase, the cleavage sites located between nucleotides encoding residues 100 and 168 of the heparanase protein.

Claim 2. (Original) A vector comprising the nucleic acid molecule of claim 1.

Claim 3. (Canceled)

Claim 4. (Original) A host cell comprising the vector of claim 3.

Claim 5. (Currently Amended) The host cell of claim 4, wherein the host cell is an insect cell or a yeast cell.

Claim 6. (Canceled)

Claim 7. (Currently Amended) The host cell of claim 6, wherein the host cell is a yeast cell which is selected from the group consisting of: *Pichia pastoris*, *Hansenula polymorpha* and *Saccharomyces cervisiae*.

Claim 8. (Original) The synthetic nucleic acid molecule of claim 1, wherein the heparanase protein is human heparanase.

Claim 9. (Original) The synthetic nucleic acid molecule of claim 8, wherein the consensus cleavage sites are located before residues G110 and K158 of the human heparanase protein.

Claim 10. (Original) The synthetic nucleic acid molecule of claim 8, wherein the consensus cleavage sites are selected from the group consisting of: tobacco etch virus (TEV) protease

cleavage sites, 3C protease cleavage sites from picornavirus, thrombin protease cleavage sites, enterokinase cleavage sites and factor Xa cleavage sites.

Claim 11. (Original) A synthetic mammalian heparanase nucleic acid molecule comprising a portion that encodes a mammalian heparanase protein, the protein coding portion consisting essentially of a sequence of nucleotides encoding an N-terminal fragment of about 8 kDa, a linker, and a sequence of nucleotides encoding a C-terminal fragment of about 50 kDa, wherein the N-terminal and C-terminal fragments encode protein fragments that are substantially similar to wild-type heparanase fragments, and wherein the encoded heparanase protein is constitutively active.

Claim 12. (Currently Amended) The gene synthetic nucleic acid molecule of claim 11, wherein the protein coding portion encodes human heparanase.

Claim 13. (Currently Amended) The gene synthetic nucleic acid molecule of claim 11, wherein the linker comprises a sequence of nucleotides that encodes a central loop region of the hyaluronidase protein.

Claim 14. (Currently Amended) The gene synthetic nucleic acid molecule of claim 13, wherein the hyaluronidase is from *H. manillensis*.

Claim 15. (Currently Amended) The gene synthetic nucleic acid molecule of claim 12, wherein the linker comprises a sequence of nucleotides that encodes a (GlySer)₃ linker.

Claim 16. (Currently Amended) A vector comprising the gene synthetic nucleic acid molecule of claim 12.

Claim 17. (Original) A host cell comprising the vector of claim 16.

Claim 18. (Original) The host cell of claim 17 which is an insect cell or a yeast cell.

Claim 19. (Original) A purified synthetic heparanase protein encoded by the gene of claim 12.

Claim 20. (Original) A method of expressing mammalian heparanase in non-mammalian cells comprising:

(a) transforming or transfecting non-mammalian cells with a vector comprising a sequence of nucleotides that encodes a mammalian heparanase protein, the sequence of nucleotides comprising two consensus cleavage sites recognized by an endoproteinase, the cleavage sites located between residues 100 and 168 of the heparanase protein;

(b) culturing the host cell under conditions which allow expression of said heparanase protein;

(c) disrupting the cells and at least partially purifying the heparanase protein; and

(d) exposing the at least partially purified heparanase protein to the endoproteinase, wherein the heparanase protein is cleaved at the consensus cleavage sites.

Claim 21. (Canceled)

Claim 22. (Original) A method of expressing a single chain, constitutively active mammalian heparanase in non-mammalian cells comprising:

(a) transforming or transfecting non-mammalian cells with a vector comprising a synthetic mammalian heparanase gene, wherein the synthetic gene comprises a portion that encodes the heparanase protein, the protein coding portion consisting essentially of a sequence of nucleotides encoding an N-terminal fragment of about 8 kDa, a sequence of nucleotides encoding a linker and a sequence of nucleotides encoding a C-terminal fragment of about 50 kDa, wherein the N-terminal and C-terminal fragments encode protein fragments that are substantially similar to wild-type fragments; and

(b) culturing the host cell under conditions which allow expression of said heparanase protein

Claim 23. (Canceled)

Claim 24. (Original) The method of claim 22 wherein the linker comprises a central (GlySer)3.

Claim 25. (Canceled)